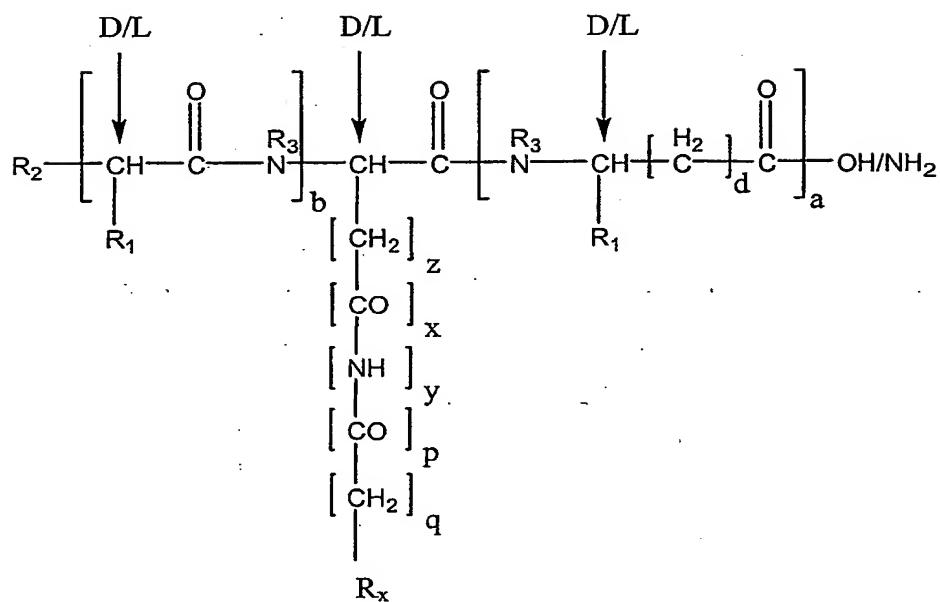


What is claimed is:

1. A peptide represented by the general formula I:



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wherein, if a is 1 then b is 0;

if a is 0 then b is 1;

wherein z is 1-7;

wherein if x is 1 then y and q are 1 and p is 0;

- 10 wherein if p is 1 then x and q are 0 and y is 1; and further, wherein,

wherein if R<sub>1</sub> is H then d is 0-8;

wherein if R<sub>1</sub> is not H then d is 0;

wherein  $R_1$  is the side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine;

5 wherein  $R_2$  is selected from the group consisting of  $NH_2$ ,  $NHR$ ,  $NR_2$ ,  $NR_3^+H$ ,  $OH$ ,  $SH$ ,  $RO$ ,  $RS$ ,  $RSO$ ,  $RSO_2$ ,  $CO_R$ ,  $CSR$ ,  $COOH$ ,  $COOR$ ,  $CONH_2$ ,  $CONHR$ ,  $CONR_2$ ,  $OCOR$ , and  $SCOR$ , wherein  $R$  = alkyl, alkenyl, aryl, aralkyl, or cycloalkyl;

wherein  $R_3$  = H or  $CH_3$ ; and

wherein  $R_x$  is a hydrophobic group.

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2. The peptide according to claim 1, wherein  $R_x$  comprises an aromatic carbon ring.

3. The peptide according to claim 2, wherein the aromatic ring comprises a 6- or 12 membered ring or a substituted form thereof.

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4. The peptide according to claim 3, wherein the ring is substituted with at least one of: a lower alkyl, alkoxy, hydroxyl, carboxy, amine, thiol, hydrazide, amide, halide, hydroxyl, ether, amine, nitrile, imine, nitro, sulfide, sulfoxide, sulfone, thiol, aldehyde, keto, carboxy, ester, an amide group; a seleno group, a thio group and derivatives thereof.

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5. The peptide according to claim 3, wherein the ring comprises about 1 to 5 substitutions.

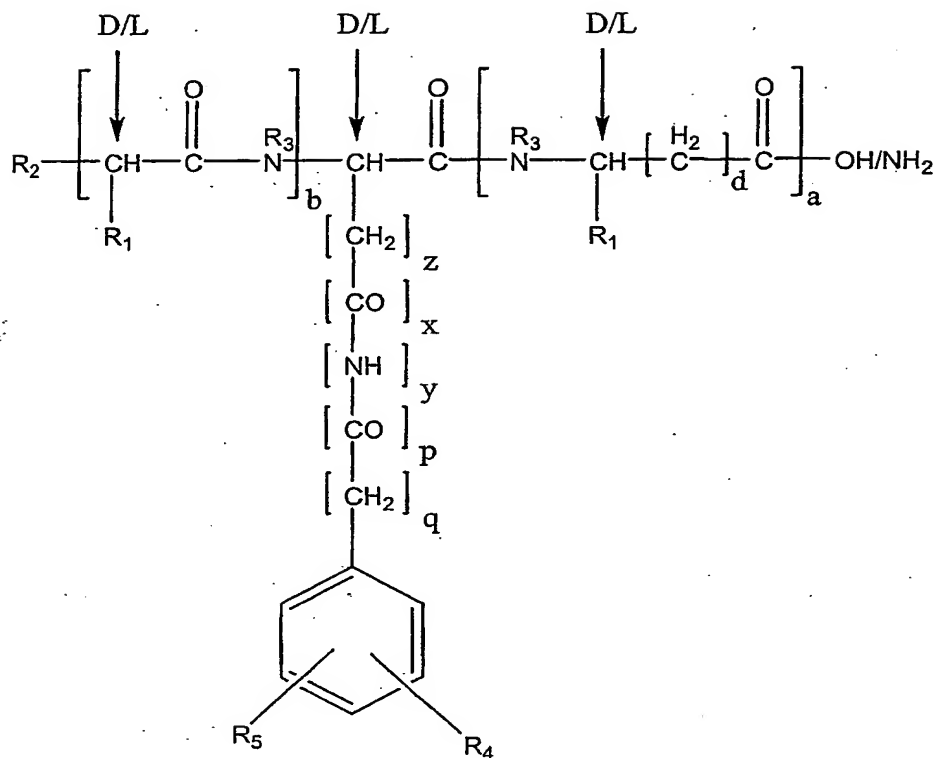
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6. The peptide according to claim 3, wherein the ring comprises about 1 to 2 substitutions.

7. The peptide according to claim 2, wherein the aromatic carbon ring is selected from the group consisting of: a benzyl, phenyl, and naphthyl group.

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8. A peptide represented by the general formula II:



wherein if a is 1 then b is 0;

if a is 0 then b is 1;

z is 1-7;

5 if x is 1 then y and q is 1 and p is 0;

if p is 1 then x and q is 0 and y is 1; and further, wherein,

if  $R_1$  is H then d is 0-8;

if  $R_1$  is not H then d is 0;

10 wherein  $R_1$  is the side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine;

15 wherein  $R_2$  is selected from the group consisting of  $NH_2$ ,  $NHR$ ,  $NR_2$ ,  $NR_3^+H$ ,  $OH$ ,  $SH$ ,  $RO$ ,  $RS$ ,  $RSO$ ,  $RSO_2$ ,  $CO_R$ ,  $CSR$ ,  $COOH$ ,  $COOR$ ,  $CONH_2$ ,  $CONHR$ ,  $CONR_2$ ,  $OCOR$ , and  $SCOR$ , wherein  $R$  = alkyl, alkenyl, aryl, aralkyl, or cycloalkyl;

wherein  $R_3$  = H or  $CH_3$ ;

wherein  $R_4$  and  $R_5$  are independently selected from the group consisting of H, alkyl, alkenyl, aryl, aralkyl, halogen, CN,  $\text{NO}_2$ , alkoxy, aryloxy, aralkyloxy, thioalkoxy, thioaryloxy, thioaralkyloxy,  $+\text{S}(\text{CH}_3)_2$ ,  $\text{SO}_3\text{H}$ ,  $\text{SO}_2\text{R}$ ,  $\text{NH}_2$ ,  $\text{NHR}$ ,  $\text{NR}_2$ ,  $+\text{NR}_3$ , OH, SH,  $\text{COOH}$ ,  $\text{COOR}$ ,  $\text{CONH}_2$ ,  $\text{CONHR}$ ,  $\text{CONR}_2$ ,  $\text{CH}_2\text{OH}$ ,  $\text{NCO}$ ,  $\text{NCOR}$ ,  $\text{NHOH}$ ,  $\text{NHNH}_2$ ,  $\text{NHNHR}$ ,  $\text{CH}_2\text{OCOR}$ ,  $\text{CH}_2\text{OCSR}$ ,  $\text{COR}$ ,  $\text{CSR}$ ,  $\text{CSOR}$ ,  $\text{CF}_3$ , and  $\text{CCl}_3$ , and wherein R is alkyl, alkenyl, aryl, aralkyl, or cycloalkyl.

9. The peptide according to claim 1 or 8, wherein the peptide comprises a free N-terminal, a free C-terminal, or both a free N- and C-terminal.
10. The peptide according to claim 1 or 8, wherein the peptide further comprises a hydrogen bond group and the distance between the mass center of the hydrogen bond group and the hydrophobic group comprises from about 4 Ångströms to about 12 Ångströms.
11. The peptide according to claim 1 or 8, wherein the peptide further comprises a hydrogen bond group and the distance between the mass center of the hydrogen bond group and the hydrophobic group comprises from about 5 Ångströms to about 10 Ångströms.
12. The peptide according to claim 1, wherein the hydrophobic group is 6-membered aromatic carbon ring comprising a substituent at the 4-position.
13. The peptide according claim 12, wherein the substituent has a radius of from about 3 to about 11 Ångströms.
14. The peptide according to claim 13, wherein the substituent is selected from the group consisting of a methyl, ethyl, t-butyl, c-hexyl, phenyl, n-butyl, n-hexyl, n-octyl, ethoxy, t-butoxy, phenoxy, butoxy, benzyloxy, n-hexyloxy, and n-octyloxy group.
15. The peptide according to any of the claims 1 or 8, wherein the peptide functions as an antiarrhythmic drug.
16. The peptide according to claim 1 or 8, wherein the peptide is an orally available peptide.

17. The peptide according to claims 1 or 8, wherein the peptide binds to an hPepT1 transporter or a biologically active fragment thereof.
18. The peptide according to claim 1 or 8, wherein the peptide has a half-life in an *in vitro* plasma stability assay of more than about 30 minutes.
- 5 19. The peptide according to claim 1 or 8, wherein the peptide has a half-life in an *in vitro* plasma stability assay of more than about 48 hours.
20. The peptide according to claim 1 or 8, wherein the peptide comprises a peptide bond that is modified to stabilize the peptide against enzymatic degradation.
21. The peptide according to claim 1 or 8, wherein the peptide binds to a tissue, cell, or  
10 cell fraction that is a site of action for an antiarrhythmic peptide.
22. The peptide according to claim 21, wherein the antiarrhythmic peptide is selected from the group consisting of AAP, AAP10, HP5, or a functional analog thereof.
23. The peptide according to claim 21, wherein the peptide is a modulator of the function of the tissue, cell, or cell fraction.
- 15 24. The peptide according to claim 23, wherein the peptide antagonizes the function of the antiarrhythmic peptide.
25. The peptide according to claim 23, wherein the peptide agonizes the function of the antiarrhythmic.
26. The peptide according to claim 21, wherein the peptide is a modulator of a receptor  
20 of the antiarrhythmic peptide.
27. The peptide according to claim 1 or 8, wherein the peptide is selected from the group consisting of the peptides shown in Table 1.
28. The peptide according to claim 1 or 8, wherein the peptide is selected from the group  
25 consisting of H-Gly-Lys(4-nitrobenzoyl)-OH (Compound 1); H-Gly-Lys(4-methoxybenzoyl)-OH (Compound 4); H-D-Lys(4-methoxybenzoyl)-Gly-OH (Compound 21); H-D-Lys(4-nitrobenzoyl)Gly-OH (Compound 22); H-D-Lys(4-t-

butylbenzoyl)-Gly-OH (Compound 54); and H-D-Asn(NH(4-nitrobenzyl)Ala-OH (Compound 96).

- 5 29. The peptide according to claim 1 or 8, wherein the peptide is selected from the group consisting of H-D-Lys(benzoyl)Gly-OH (Compound 23) and H-D-Asn(NH(4-methoxybenzyl)Ala-OH (Compound 95).
30. The peptide according to claim 1 or 8, wherein the peptide is H-Gly-Lys(4-nitrobenzoyl)-OH (Compound 1).
31. The peptide according to claim 1 or 8, wherein the peptide is H-Gly-Lys(4-methoxybenzoyl)-OH (Compound 4).
- 10 32. The peptide according to claim 1 or 8, wherein the peptide is H-D-Lys(4-methoxybenzoyl)-Gly-OH (Compound 21).
33. The peptide according to claim 1 or 8, wherein the peptide is H-D-Lys(4-nitrobenzoyl)Gly-OH (Compound 22).
- 15 34. The peptide according to the claims 1 or 8, wherein the peptide is H-D-Lys(4-t-butylbenzoyl)-Gly-OH (Compound 54).
35. The peptide according to the claims 1 or 8, wherein the peptide is H-D-Asn(NH(4-nitrobenzyl)Ala-OH (Compound 96).
36. The peptide according to claim 1 or 8, wherein the peptide is H-D-Lys(benzoyl)Gly-OH (Compound 23).
- 20 37. The peptide according to claim 1 or 8, wherein the peptide is H-D-Asn(NH(4-methoxybenzyl)Ala-OH (Compound 95).
38. The peptide according to any of the preceding claims, wherein the peptide comprises a free N-terminal, a free C-terminal or both a free N- and C-terminal.
- 25 39. A method for modulating gap junctional communication in a population of cells comprising administering an effective amount of a peptide according to claim 1 or 8

to the population of cells thereby modulating gap junctional communication between the cells.

40. The method according to claim 39, wherein administering is performed *in vivo*.
41. A method of treating a patient having, or at risk of developing, a pathological condition involving impaired gap junctional communication comprising administering to the patient a therapeutically effective amount of a peptide according to claim 1 or 8.
42. The method according to claim 41, wherein administration is oral.
43. The method according to claim 41, wherein the patient is a human being.
44. The method according to claim 41, wherein the pathological condition is selected from the group consisting of a cardiovascular disease, inflammation of airway epithelium, a disorder of alveolar tissue, bladder incontinence, impaired hearing, an endothelial lesion, diabetic retinopathy, diabetic neuropathy, ischemia of the central nervous system, ischemia of the spinal cord, a dental tissue disorder, kidney disease, failure of bone marrow transplantation, wound, erectile dysfunction, urinary bladder incontinence, neuropathic pain, subchronic and chronic inflammation, cancer, transplantation failure; a condition caused by an excess of reactive oxygen species and/or free radicals and/or nitric oxide.
45. A method for modulating gap junctional communication in a population of cells comprising administering an effective amount of a peptide according to claim 1 or 8 to the population of cells thereby modulating gap junctional communication between the cells.
46. The method according to claim 45, wherein administering is performed *in vivo*.
47. Use of a peptide according to the claims 1-38 for the manufacture of a medicament for the treatment of a pathological condition involving impaired gap junctional communication comprising administering to a patient a therapeutically effective amount of said peptide.

48. The use according to claim 47, wherein the administration is oral.
49. The use according to claim 47, wherein the patient is a human being.
50. The use according to claim 47, wherein the pathological condition is selected from the group consisting of a cardiovascular disease, inflammation of airway epithelium, a disorder of alveolar tissue, bladder incontinence, impaired hearing, an endothelial lesion, diabetic retinopathy, diabetic neuropathy, ischemia of the central nervous system, ischemia of the spinal cord, a dental tissue disorder, kidney disease, failure of bone marrow transplantation, wound, erectile dysfunction, urinary bladder incontinence, neuropathic pain, subchronic and chronic inflammation, cancer, transplantation failure; a condition caused by an excess of reactive oxygen species and/or free radicals and/or nitric oxide.
51. A pharmaceutical composition comprising the peptide of the claims 1-38 and a pharmaceutical carrier.
52. The pharmaceutical composition according to claim 51, wherein the composition is orally administrable.